(3WJ) motif. In some embodiments of the present disclosure, the RNA molecules form dimers, trimers, hexamers, and patterned superstructures.

[0012] In some embodiments, the presently disclosed subject matter provides that a branch of the three-branched RNA junction motif includes an a3WJ RNA module. In some embodiments, a branch of the three-branched RNA junction motif includes a b3WJ RNA module. In some embodiments, a branch of the three-branched RNA junction motif includes a c3WJ RNA module. In some embodiments, the three-branched RNA junction motif includes an a3WJ RNA module, a b3WJ RNA module, and a c3WJ RNA module. A non-limiting example of RNA module include nucleotide sequences 5'-UUG CCA UGU GUA UGU GGG-3' (SEQ ID NO: 1), 5'-CCC ACA UAC UUU GUU GAUCC-3' (SEQ ID NO: 2), and 5'-GGA UCA AUC AUG GCA A-3' (SEQ ID NO: 3).

[0013] In some embodiments, the diameter of the molecule is at least about 40 nm or less. In some embodiments, the diameter of the molecule is at least about 30 nm or less. In some embodiments, the diameter of the molecule is at least about 15 nm or less.

[0014] In some embodiments, the RNA molecule has a zeta potential ranging from about −50 mV to about 50 mV. In some embodiments, the molecule has a zeta potential ranging from about −25 my to about 25 mV.

[0015] In some embodiments, the presently disclosed subject matter provides that the brain tumor targeting module in the artificial RNA nanostructure molecule includes a ligand that binds to at least one brain tumor cell surface marker. Non-limiting examples of the brain tumor surface marker includes folate receptor, EGFR, transferrin receptor, and an RGD. In some embodiments, the ligand includes an aptamer. In some embodiments, the aptamer binds to EGFR, PDGFR, folate receptor, or a combination thereof. In some embodiments, In some embodiments, the targeting module is a folate.

[0016] In some embodiments, the presently disclosed subject matter provides a bioactive agent includes a drug, a fluorescent dye, a chemical, or a combination thereof. In some embodiments, the bioactive agent includes a siRNA, a miRNA, an anti-miRNA, a ribozyme RNA, an antisense RNA, or a combination thereof In some embodiments, the bioactive agent is directed to a brain tumor marker. Non-limiting examples of the bioactive agent include siRNA sequence and microRNA sequence. In some embodiments, the microRNA molecule is at least 3 nucleotide in length. In some embodiments, the bioactive agent is an anti-miRNA molecule for a miRNA encoding miR-9, miR-10b, miR-21, miR-17, or miR-26. In some embodiments, the bioactive agent is a miRNA molecule for a miRNA encoding let-7a, miR-10b, miR-25, miR-34a, miR-124, miR-145, or miR-181b. In some embodiments, the miRNA includes miRNA locked nucleic acid (LNA) molecule. In some embodiments, the microRNA sequence is an anti-miR-21 sequence. In some embodiments, non-limiting examples of the miRNA sequence comprises 5'-GATAAGCT-3',5'-AGCACTTT-3', or 5'-ATTTGCAC-3'. In some embodiments, the miRNA includes an miRNA locked nucleic acid (LNA) molecule. In some embodiments, the bioactive agent includes a LNA miRNA molecule 5'-+G+A+T+A+A+G+C+T-3'. In some embodiments, miRNA LNA molecule includes a sequence 5'-+A+G+C+A+C+T+T+T-3'. In some embodiments, miRNA LNA molecule includes a sequence 5'-+A+T+T+T+G+C+A+C-3'.

[0017] In some embodiments, the microRNA is a locked nucleic acid (LNA) sequence. In some embodiments, the microRNA is a LNA-miR21 sequence 5'-+G+A+T+A+A+G+C+T-3'. In some embodiments, the siRNA binds to a mRNA sequence of a gene that promotes tumorigenesis, angiogenesis, cell proliferation, or a combination thereof, in the brain or spinal cord. In some embodiments, the siRNA binds to a mRNA molecule that encodes a protein including pro-tumorigenic pathway proteins, pro- angiogenesis pathway proteins, pro-cell proliferation pathway proteins, anti-apoptotic pathway proteins, or a combination thereof. In further embodiments, the mRNA molecule encodes a protein including but not limited to VEGF pathway proteins, EGFR pathway proteins, MGMT pathway proteins, Rafl pathway proteins, MMP pathway proteins, mTOR pathway proteins, TGFβ pathway proteins, or Cox-2 pathway proteins, or a combination thereof. In some embodiments, non-limiting examples of protein include VEGF, EGFR, POK, AKT, AGT, RAF, RAS, MAPK, ERK, MGMT, MMP-2, MMP-9, PDGF, PDGFR, IGF-I, HGF, mTOR, Cox-2 and TGFβ1. In some embodiments, the siRNa binds to a mRNA molecule that encodes RAS, cMET, HER2, MDM2, PIK3CA, AKT, CDK4, or a combination thereof.

[0018] Further provided, in some embodiments of the presently disclosed subject matter, is a nucleic acid composition. The composition includes a therapeutically effective amount of the artificial RNA nanostructure molecule as disclosed above. In some embodiments, the composition includes a pharmaceutically acceptable carrier.

[0019] Still further, the presently disclosed subject matter, in some embodiments, provides a nanoparticle delivery system. The delivery system includes the artificial RNA nanostructure molecule as disclosed above. In some embodiments, the nanoparticle delivery system further includes a pharmaceutically acceptable carrier.

[0020] In another aspect, the presently disclosed subject matter provides, in some embodiments, a method of treating a brain tumor in a subject having or at risk of developing a brain tumor. The method includes administering to the subject a therapeutically effective amount of a composition comprising an artificial RNA nanostructure molecule as disclosed herein. In some embodiments, the composition includes a pharmaceutically acceptable carrier. In some embodiments, the subject is a mammal or a non-mammal vertebrate. In some embodiments, the subject is a human. In some embodiments, the brain tumor is glioblastoma.

[0021] Further, in some embodiments, the present disclosure provides a method of preventing brain tumor recurrence a subject having or at risk of having brain tumor recurrence. The method includes administering to the subject a therapeutically effective amount of a composition comprising an artificial RNA nanostructure molecule as disclosed herein. In some embodiments, the composition includes a pharmaceutically acceptable carrier. In some embodiments, the subject is a mammal or a non-mammal vertebrate. In some embodiments, the subject is a human. In some embodiments, the brain tumor is glioblastoma.

BRIEF DESCRIPTION OF THE DRAWINGS

[0022] The features of the presently disclosed subject matter are set forth with particularity in the appended claims.